SEX DETERMINATION

F. A. E. CREW

ETHUEN'S MONOGRAPHS ON
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General Editor: MICHAEL ABERCROMBIE

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PREFACE

THE purpose of this book is to present the salient facts relating to sex-determination and to guide the student to further reading. It presupposes that the reader already has a fair knowledge of genetics and cytology; it restricts itself to a consideration of the cytological and genetical aspects of sex-determination and does not consider the problems that cluster round the actual development of the sexual characters, since such development pertains not to sex-determination but rather to sex-differentiation.

Those who wish to explore more fully the matters touched upon in this book are advised to turn to *Advances in Genetics*, edited by M. Demerec, four volumes of which have been published so far in 1947–1951 by Academic Press Incorporated, New York, and to *The Evolution of Genetic Systems* by C. D. Darlington, published in 1946 by the Cambridge University Press. Such as wish to proceed from a study of sex-determination to one of sex-differentiation can profitably refer to F. H. A. Marshall's *Physiology of Reproduction*, third edition, edited by A. S. Parkes and published in 1952 by Longmans, Green, London, or to *Sex and Internal Secretions*, edited by Edgar Allen and published in 1939 by Williams and Wilkins Company, Baltimore.

F. A. E. C.

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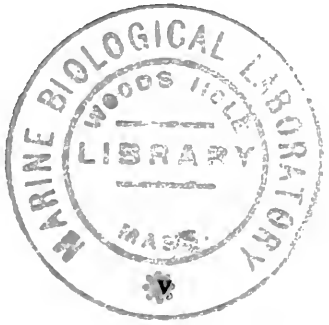

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CHAPTER I

THE GENETIC THEORY OF SEX-DETERMINATION

Sex (L. *seco*, to cut), the distinction between male and female, the property by which an individual is male or female. Sexuality, the quality of being distinguished by sex.

FROM the very beginning of human existence a difference between the two contrasted types we know as male and female respectively must have been recognized. Within every individual the force of sexuality has operated to focus thought upon matters sexual and to yield an intense awareness of the sexually contrasted form. It can safely be assumed that this observed difference in mankind and in the animals man domesticated has at all times intrigued the human mind and provoked speculation concerning its significance and causation. Every individual displays the property of sexuality and by his own experience knows of it. Speculation concerning it has never been restricted to students of biology; any man can claim to be his own authority.

The observations that required an explanation were but few to begin with. Maleness and femaleness were attributes which were exercised in the sexual relationship. The sexual union of male and female resulted in reproduction, in the production of offspring among whom males and females appeared in more or less equal numbers. In this production by a male and a female of males and females there was to be observed an orderliness and a precision which suggested that some relatively simple mechanism was involved.

Hypotheses concerning the way in which and the time during the life history of the individual at which sex is determined have been plentiful. For the most part they were elaborated at a time when little or nothing was known of the anatomy and physiology of the cell, of cell division, of gametogenesis and of fertilization, or they were constructed by such as were unaware of, or chose to disregard, what was

known concerning these matters. Up to the beginning of the present century each of them in its turn was destroyed when it proved to be incapable of accommodating some new observation. In retrospect it is easy to understand how it came about that a theory derived from and based upon the experience of an obstetrician, for example, could not be stretched to include the outcome of the experience of a breeder of habitually polytocous livestock.

Then, as the studies of the zoologist and of the botanist widened to include an ever-expanding number of species, it is understandable how it happened that a theory elaborated by a zoologist proved to be of no value whatsoever to a botanist who had encountered in his material phenomena strongly resembling those of sexuality in the animal. That for which men continually sought was a theory that could accommodate all that was known about the phenomenon of sexuality wherever it appeared, and as this knowledge expanded the difficulties of constructing a satisfactory theory of the causation of sex multiplied.

Each of these theories of sex-determination has to be examined against the background of the total biological knowledge that was in man's possession at the time when the theory was promulgated. If it accommodated all the observations thus far made, and if it was a reasonable, intelligent groping after understanding, then in its day it was a good and useful theory. That it is now unwarrantable in the light of our vastly increased knowledge of matters biological in no way robs the theory of its merit.

By the beginning of this century our knowledge of the cell, of gametogenesis and of fertilization had become greatly expanded, and in the earliest years of the century, as an outcome of the confirmation of the Mendelian theory of organic inheritance, much attention became focused upon the mode of transmission of inherited characters and the search began for the actual mechanism of segregation that was postulated by the Mendelian theory. Thus it was that the sciences of genetics and of cytology entered into a phase of intensely active development.

The facts to be accommodated by a theory of sex-

determination could now be stated more exactly. In a wide variety of species sex-dimorphism occurs; within them there are males and females. Sexual reproduction, taking the form of the fusion, permanently or temporarily, of two complete individuals or parts thereof or in the union of single cells derived from one and the same individual or from two individuals, occurs in all those groups of organisms in which the presence of a nucleus has been demonstrated. In the higher forms sexual reproduction consists in the formation of single cells, the gametes, the separation of these from the rest of the individual and their subsequent fusion in pairs to form the zygotes, the new individuals of a new generation. In most of these forms two kinds of gametes are to be found—a small, active, motile gamete elaborated by the male (or by the testis of the hermaphrodite) and a relatively large, inactive, non-motile gamete elaborated by the female (or by the ovary of the hermaphrodite). These gametes constitute the only organic bridge connecting the generations.

Usually during spermatogenesis the nucleus and the cytoplasm of a cell are equally divided among four functional spermatozoa, whilst during oogenesis three of the products of division are suppressed and extruded to become the polar bodies, only one remaining to become the functional ovum.

The simplest form of spermatozoon consists of four parts: (1) the nucleus forming the head; (2) the centrosome, a non-nuclear body forming the middle piece from which the axial filament of the vibratile tail is developed; (3) the mitochondria, bodies of non-nuclear origin which form the sheath of this filament, and (4) ordinary cytoplasm which forms a thin coat over the head and tail. The nucleus alone is the constant constituent of the spermatozoon; it alone fuses with the nucleus of the ovum. No other organ save the centrosome takes any part in the development of the new individual.

The essential feature of sexuality is the production of two different kinds of gametes by the individuals of a species, male-type by the male, female-type by the female. Fusion between gametes is restricted to such as possess and display

contrasted characters (details of structure and of behaviour), and usually to such as are derived from two sexually contrasted individuals.

The division of a cell into two by simple fission is no mere casual cleavage; it is a process of precision, karyokinesis or mitosis, the essential feature of which is the exact halving of the two chief constituents of the cell, the nucleus and the cytoplasm, so that the two daughter cells that result are, save in respect of initial size, exact copies of the cell that produced them.

The most striking features of mitosis are the exact and precise division of the chromosomes and the precise distribution of the daughter chromosomes so formed. In respect of their chromosome constitution the daughter cells are exact copies of the mother cell that produced them.

In each and every species there is a characteristic number of chromosomes within the nuclei of its component cells. For example, man has forty-eight (Evans and Swezy, 1929). These exist in the form of pairs, the members of any given pair (with one exception later to be considered) being alike in size, shape and behaviour during cell-division.

This constancy of the chromosome number could not exist if at fertilization both the egg and the sperm brought into the new zygote that number of chromosomes which is characteristic of the species. Offspring have the same number as the parents (polymitotic forms and polyploidy being disregarded). Constancy is maintained by a reduction of the chromosome number to a half during gametogenesis. The existence of this process was postulated by Weismann (1887). His hypothesis has been verified universally since then. Wherever there is fertilization there is also reduction, which in essence consists of two divisions of the nucleus of the cell associated with one division of its chromosomes, with the result that four daughter nuclei are produced, each of these having half the number (the haploid number) of chromosomes characteristic of the species. Meiosis, this process of reduction, is a modification of mitosis.

Fertilization consists essentially in the bringing together of two half-sets of chromosomes and the consequent re-

establishment of the characteristic chromosome number. One member of each of the pairs of chromosomes with which the new individual is endowed comes by way of the spermatozoon from the father; its mate comes by way of the ovum from the mother.

Many of the details of structure and function that are exhibited by the individual are the expression of the hereditary constitution of the individual. Mendel postulated that such characters were brought into being by the action of 'hereditary factors'. In every individual's constitution, and in respect of any given character, there were two such factors, only one of which passed into each gamete. Commonly, of the pair of hereditary factors one was dominant, the other recessive, the dominant one alone exerting an influence during development. Thus an individual exhibiting the dominant member of a contrasted pair of hereditary characters could be either a homozygous dominant (DD) or else a heterozygous dominant (Dd).

Mendel (1865) himself hazarded the suggestion that sex-determination might prove to be a phenomenon of heredity and segregation. Experimental evidence of its validity was furnished as early as 1907 by Correns, who studied hybrids between monoecious and dioecious species of Bryonia. His results indicated that in the dioecious species sex was determined by the pollen grain of which there were two kinds equal in number, one being male-producing and the other female-producing whilst the ovules were all of a kind. Correns compared the combinations resulting from the union of the two forms of pollen grain with the one form of ovule with those of the typical back-cross of a Mendelian experiment in which the heterozygous dominant (Dd) mated to a recessive (dd) yields equal numbers of heterozygous dominants and recessives.

	Dd	×		dd	
D		d	:	d	gametes
Dd		:		dd	

Doncaster (1906), working with the currant moth *Abraxas grossulariata*, produced evidence that strongly suggested

that in animals also sex-determination was due to segregation of hereditary factors.

Bateson and Punnett (1908), basing their interpretation on the assumption that the character femaleness was dominant to the contrasted character maleness, and that the female in Abraxas was always heterozygous in respect of the character femaleness, devised a scheme, of considerable historical interest, to show the relationship of the sex of the individual to its colour pattern. If the hereditary factor for the grossulariata colour pattern is symbolized by G, that for lactocolor by g, that for the dominant femaleness character by F, and that for the recessive maleness character by f, then the results of Doncaster's experiments can easily be accommodated, if it is assumed that the female is always constitutionally heterozygous (Ff) for the character femaleness, and further, that the two dominant factors G and F repel each other so that they can never be present together in the same gamete.

The results of the breeding experiments carried out by Doncaster were as follows:

1. lacticolor ♀ × gross. ♂=gross. sons and daughters. Gross. was dominant to lacticolor.
   In the F.2 both gross. and lact. occurred, there being on the average in every 4, 3 gross. to 1 lact. Among the gross. individuals there were both males and females but the lacticolors were all females.
2. F.1 gross. ♂ × lact. ♀=gross. and lact. individuals in equal numbers and among both of these types males and females in equal numbers.
3. lact. ♂ from 2 × F.1 gross. ♀=equal numbers of gross. and lact. individuals but all the gross. were males and all the lact. were females.
4. lact. ♂ from 2 × wild gross. ♀=equal numbers of gross. and lact. individuals but all gross. were males and all lact, were females.

Bateson and Punnett's explanation of these results was as follows:

1.	lact. ♀	×	gross. ♂	
	ggFf		GGff	P.1
	gF gf	:	Gf	gametes
	GgFf		Ggff	F.1
	gross. ♀		gross. ♂	

Gf gF (repulsion) : Gf gf gametes
GGff Ggff GgFf ggFf F.2
gross. ♂ gross. ♂ gross. ♀ lact. ♀

2. lact. ♀ × F.1 gross. ♂
ggFf Ggff
gF gf : Gf gf gametes
GgFf ggFf Ggff ggff
gross. ♀ lact. ♀ gross. ♂ lact. ♀

3. F.1 gross. ♀ × lact. ♂
GgFf ggff
Gf gF (repulsion) : gf gametes
Ggff ggFf
gross. ♂ lact. ♀

4. wild gross. ♀ × lact. ♂
GgFf ggff
Gf gF (repulsion) : gf gametes
Ggff ggFf
gross. ♂ lact. ♀

Since the time when this explanation of what is now known to be an instance of the inheritance of sex-linked characters was offered, the sciences of cytology and genetics have expanded vastly and out of their development emerged the current theory of sex-determination. By this theory all the older hypotheses of sex-determination have been rendered obsolete and, save for historical purposes, can be disregarded. The framework of this theory consists of secure knowledge concerning the constant and significant differences between male and female in respect of their sex-chromosome and therefore of their genic constitution and, secondly, concerning the observed facts relating to the phenomenon of sex-linkage, which enables the observer to trace the transmission of sex-chromosomes from generation to generation. The primary difference between the sexes is now known to be a chromosomal and a genic difference. In the bisexual and dioecious species the sex of the individual, as a general rule, is now known to be decided at the moment of fertilization by the interplay of the sex-chromosome constitutions of the uniting gametes. This chromosomal,

genetic, theory was confirmed by the correlation that has been observed between the distribution in inheritance of the sex-chromosomes and of the sex-linked characters. Nothing that has been encountered during the last fifty years has required any significant modification of this theory. At present it seems distinctly unlikely that this theory will be at all seriously shaken in foreseeable time, but new discovery in other scientific fields may, in its impact upon biological science, necessitate its review and revision.

CHAPTER 2

THE SEX-CHROMOSOMES AND SEX-DETERMINATION

In a very large number and in a wide variety of species it has been shown that the male is to be distinguished from the female by constant differences in the chromosome content of the nuclei of their component cells. This difference takes several forms. In certain species one sex possesses one chromosome less than does the other, that is to say in one sex the chromosomes are all paired whilst in the other one member of one pair is lacking. In other species both sexes possess the same number of chromosomes, existing in pairs, but in one sex one particular pair consists of chromosomes unequal in size and shape.

The single unpaired chromosome found in one sex and the pair in the other to which it corresponds, and the pair of chromosomes in respect of which the sexes differ, are known as the sex-chromosomes in order to distinguish them from the rest of the chromosomes in respect of which both male and female are alike. These are known as the autosomes. The single chromosome found in one sex and the pair in the other to which it corresponds and, in the case of the species in which the chromosome number is the same in both sexes, that chromosome which is found in both male and female, are known as X-chromosomes. The unequal mate of the X in one of the sexes is known as the Y-chromosome. Thus in respect of sex-chromosome constitution the sexes can be described as:

XO:XX
or XY:XX

The third form which this difference between the sexes takes is that in which the sex-chromosomes are represented not by single elements but by groups which during gametogenesis behave as one compound chromosome. Whatever

the number of X-chromosomes within the group, the group itself is single in one sex, double in the other, so that essentially this difference is of the XO:XX type or, as is sometimes the case, XY:XX, for the single compound X is in certain species associated with a Y-chromosome. Ray-Chaudhuri and Manna (1950) report that the male of the gryllid Euscyrtus is X^1X^2Y. The Y can itself be compound. Thus in the dioecious plant *Rumex acetosa* Kihara and Ono (1923) found a Y-chromosome consisting of two elements in association with a single X. According to Sharman, McIntosh and Barber (1950) the rat kangaroo is XY^1Y^2 in the male, XX in the female.

The first account of a sex-chromosome difference was that of Henking (1891), who described in the bug *Pyrrhocoris apterus* a peculiar chromatin element which was condensed in the early prophase of the primary spermatocyte. In the first spermatocyte division the twelve elements found in the metaphase plate all divided equally, but in the second division one of the twelve elements lagged and finally passed undivided into one of the two daughter cells. As a result two kinds of spermatids were formed, one with eleven and one with twelve of these elements. Henking did not at this time refer to this odd chromatin element as a chromosome but called it a 'nucleolus'. He did not confuse it with a true nucleolus, however.

In 1898 Paulmier recorded a similar phenomenon in *Anasa tristis*, in the second spermatocyte division of which eleven chromosomes passed to one pole and ten to the other. In 1901 de Sinety described the behaviour of what he called a 'chromosome spécial' in the male of Orphania. In the same year McClung suggested that the two classes of spermatozoa resulting from the meiotic distribution of the 'accessory' chromosome must be causally related to the production of the two sexes. 'Upon the assumption that there is a qualitative difference between the various chromosomes of the nucleus it would necessarily follow that there are formed two kinds of spermatozoa which, by fertilization of the egg, would produce individuals qualitatively different. Since the number of each of these varieties of spermatozoa

is the same, it would happen that there would be an approximately equal number of these two kinds of offspring. We know that the only quality which separates the members of the species into these two groups is that of sex.'

Thus it was that the chromosome complex came to be associated with sex-determination. McClung's main hypothesis was complicated by its association with a subsidiary one of selective fertilization which led him to the conclusion that the spermatozoon carrying the extra chromosome was male-determining. If this were so, then the male had to be the sex which had one chromosome more than did the female. Sutton (1902), by reporting that the spermatogonia of Brachystola possessed one chromosome more than did the ovarian follicle cells, provided support for McClung's error.

The work of McClung aroused great interest and much controversy. It evoked great activity in the field of cytology. Gross (1906) claimed to have demonstrated that in Syromastes and Pyrrhocoris the accessory chromosome (the single, unpaired one) present in the spermatocytes arose from two small spermatogonial chromosomes and, further, that the number of chromosomes was the same for both sexes. It was his opinion that all spermatozoa lacking the accessory chromosome degenerated so that only one type of functional gamete remained. However, Stevens (1905) in the beetle Tenebrio and Wilson (1905) in the bug *Lygaeus furcicus* showed clearly that in these forms at least there was one pair of unequal chromosomes and that this pair behaved in the growth stages of the spermatocytes exactly like the unpaired accessory chromosome. They found also that the members of this unequal pair separated and passed to opposite poles in one of the two meiotic divisions. Stevens further demonstrated that the diploid number of chromosomes was the same in both sexes but that in the female no pair consisting of unequal mates was present, the male being XY, the female XX. Then in 1909 Wilson corrected Gross by showing that in the male of Pyrrhocoris there was an unpaired chromosome in the spermatocyte and that this arose from a single spermatogonial chromosome of corresponding

size and not, as Gross thought, from a pair of smaller spermatogonial chromosomes. In the case of Syromastes Wilson showed that Gross was correct in his observation that these two chromosomes represented the components of a compound sex-chromosome which was unpaired. In the female each of the two components was represented twice so that the diploid number was greater by two chromosomes than was that of the male.

It thus appeared that the X-chromosome was the sex-determining agent, one X yielding a male, two XX's a female, the Y-chromosome itself exerting no discernible influence. This heterogamety on the part of the male and this homogamety on the part of the female were responsible for the production of a sex-ratio of equality in the next generation.

Male		Female	
X–		XX	
X	– :	X	gametes (two forms of spermatozoa, one form of ova)
XX		X–	fertilization
Females in equal numbers		Males	

The XO=male; XX=female type of sex-determining mechanism is commonly known as the 'Protenor type'. In this form the male is the heterogametic sex. Half of the spermatozoa produced by the male contain one X-chromosome and are female-producing, while the other half lack such a chromosome and are male-producing. The diploid chromosome number in the female is a multiple of two; the chromosome number in the male is one less. In *Protenor belfragi* the diploid number in the female is 14, whilst in the male it is 13. Since in this species the X-chromosome is at least twice the size of any of the autosomes it is readily recognized. The single X-chromosome of the male is always derived by way of the egg from the mother, passes from the male to the female in the production of females and from the female to the male in the production of males.

The fact that in maturation each ovum received a single

X-chromosome was first established through the work of Morrill (1910) on the maturation of the egg in various hemiptera, of Boveri (1909) and Gulick (1911) on the nematode Heterakis and of Mulsow (1912) on the nematode *Ancyracanthus cystidicola*. In the last of these forms the chromosomes remain separate in the spermatozoon so that they can be counted. The primordial egg cells in the ovary contain 12 chromosomes. During synapsis 6 double elements are to be seen. The first maturation division removes 6 complete chromosomes from the egg into the polar body; the second maturation division splits each remaining chromosome longitudinally and separates the resulting halves. The mature egg therefore comes to possess 6 chromosomes, one of these being the X.

In the case of the male gamete the primordial germ cells of the testis include only 11 chromosomes, one of which is the unpaired X. When these chromosomes conjugate in the synapsis stage the X-chromosome has no partner and it remains apart from the others in the resting nucleus. In the first maturation division there are 5 bivalent chromosomes and the univalent X. When the chromosomes are distributed to the daughter cells the X passes undivided to one of these. This heterotypic division yields two primary spermatocytes, one with 5 chromosomes, the other 6. The homotypic division cleaves each of these primary spermatocytes into two by ordinary mitosis with the result that four spermatids are formed, two of them with 5 and two with 6 chromosomes. During their maturation into spermatozoa the chromosomes remain visible and it is possible to observe that the eggs are fertilized by 5 chromosomes and 6 chromosomes bearing spermatozoa respectively.

Later cytological work showed that the Protenor type is to be found in most orthopterans, many bugs, beetles, spiders, myriapods and nematodes. Hughes-Schrader (1947), for example, lists 17 species of the bisexual Phasmids which are XO in the male.

The Lygaeus type is commonly regarded as a more primitive form from which the Protenor type was derived through the progressive loss of the Y-chromosome. It is

characterized by the presence of a synaptic mate for the X. The diploid number of chromosomes is the same in both sexes.

Male		Female	
XY	×	XX	
X Y	:	X	gametes
XX	:	XY	fertilization
Females		Males	

in equal numbers

All the mature ova of the female receive a single X. The Y is strictly confined to the male line. The son receives his Y from his father and his X from his mother. The daughter receives one X from each of her parents.

The Y commonly, though by no means invariably, is smaller than the X. In the majority of instances the X and the Y are disjoined in the first or heterotypic division, each dividing equationally in the homotypic division. During the growth period of the spermatocytes both the X and the Y typically undergo heteropycnosis and in most instances they unite to form a single bivalent. This then separates into its two components so that half the sperm receive an X, the other half a Y.

The XY pair differs from the autosomes in that they usually do not take part in the synaptotene stages or in the formation of tetrads. There is a tendency for the X and the Y to come together during prophase. In many instances their contact is but slight so that the two chromosomes can still be distinguished. In other cases the union which occurs during the growth stages of the meiotic period is a much more intimate one and the two chromosomes are contained within a single chromosome nucleolus. The joined X and Y may enter into the primary spermatocyte spindle in the form of a tetrad. But the inequality of the X and Y can usually be recognized in these structures and therefore the presence of a tetrad does not necessarily indicate any actual synapsis.

The Lygaeus type of sex-chromosome sex-determining mechanism is to be encountered in mammals and dioecious plants, is common in diptera and not unusual in bugs and beetles. The size difference between the X and the Y varies

greatly from species to species; the Y may be exceedingly small or it can be equal in size to the X. Among the bugs there are species which can be graded according to the relative size of the Y, from those in which the Y is as large as the X to those in which the Y is absent.

Hetero- or di-gamety is not a property of the male, however. In birds and lepidoptera it is the female that is heterogametic and the male that is homogametic.

The male of the domestic fowl has an even number of matched chromosomes, including seven pairs of large ones and fifteen pairs of small ones. Sokolow, Tiniakow and Trofimov (1936) concluded that the sex-chromosome was a V-shaped chromosome with arms of equal length which was present in duplicate in the male and in the simplex state in the female. They found it impossible to decide whether or not one or other of the many small chromosomes was the Y in the female. Pheasants, peafowl and turkeys were found to have the same kind of sex-chromosome constitution. In the guinea-fowl and woodcock there were two such chromosomes in the female, four in the male.

Among the lepidoptera Seiler (1920) found in the moth *Talaeporia tubulosa* 60 matched chromosomes in the male and 59 in the female which synapsed into 29 pairs and an unpaired univalent.

The difference between male and female heterogamety in no way affects the functioning of the mechanism.

Male		Female		
XX	×	XO or XY		
X	:	X or X	O Y	gametes
XX	:	XO or XY		fertilization
Males		Females		

The compound sex-chromosome mechanism has been encountered in Tenodera, Paratenodera, Mantis, Stagmomantis and in Hierodula, the males being X_1X_2Y and the females $X_1X_1X_2X_2$ (Oguma, 1921; King, 1931; Asana, 1934). More recent work (White, 1938, 1941; Hughes-Schrader,

1943, 1948, 1950; Matthey, 1949; Oguma, 1946) has shown that not all the Praying Mantis have this type of sex-chromosome mechanism, the males of many genera being XO. It has been suggested (White, 1941; Hughes-Schrader, 1950) that the compound type arose from the more primitive XO type through a structural rearrangement or series of rearrangements. Possibly a single mutual translocation between a metacentric X and a metacentric autosome converted the original XO mechanism into the X_1X_2Y mechanism without any intermediate steps. If this is so, then the Y is the homologue of the autosome involved in the translocation. In the grasshopper *Paratylotropidia brunneri* King and Beams (1938) found the sex-chromosome mechanism likewise to be X_1X_2Y=male, $X_1X_1X_2X_2$=female.

The Sex-Ratio. The homo- heterogametic mechanism described above should yield a sex-ratio among the newly conceived, a primary sex-ratio, of equality. This numerical relationship of males and females is expressed either as so many males per 100 or per 1,000 females within the group or else as the percentage of males among all the newly conceived. It is impossible to determine the primary sex-ratio among such forms as fishes, birds and mammals by direct observation. It is necessary to examine a sufficient number of foetuses and embryos as near to the point in their development at which the differences that distinguish the sexes can be recognized. When this is done it is found that the sex-ratio among them is not one of equality though not far removed therefrom. This 'foetal' sex-ratio ranges from 44·5 per cent. males in some of these studies to 56·8 in others. (*Handbook of Biological Data.*)

These observations do not destroy the validity of the argument concerning the homo- heterogametic mechanism. They are to be explained in different instances by one or other of the following phenomena:

1. The two forms of gametes elaborated by the heterogametic sex are not always produced in equal numbers.
2. These two forms are not invariably equally efficient fertilization.

3. The two forms of zygote resulting from fertilization are not always equally viable so that almost from the beginning a sexually selective mortality operates to produce a sex-ratio of inequality among the products of conception and therefore among the newly-born (the secondary sex-ratio).

CHAPTER 3

SEX-LINKAGE. NON-DISJUNCTION GYNANDROMORPHISM

Sex-Linkage. When describing the transmission of a character from parent to offspring it is not necessary in the great majority of instances to make any reference to the sex of the parent or of the offspring; it is enough to state that, for example, the dominant character exhibited by one of the parents is displayed by all or by 50 per cent. of the offspring, or that the recessive character exhibited by one of the grandparents reappears in approximately 25 per cent. of the grandchildren. In certain instances, however, like that of the grossulariata and lacticolor characters of Abraxas, a correct description involves reference not only to the distribution of these characters among the individuals of the different generations but also to the sex of the individuals that display these characters.

Although the exact chromosome constitution of Abraxas is unknown, the results obtained by Doncaster can be most easily explained as follows. Assume that Abraxas has the Lygaeus type of sex-chromosome constitution, that the female is the heterogametic sex, that the genes for the characters grossulariata and lacticolor are resident in the X-chromosome (in any one X there being either that for grossulariata or else that for lacticolor), and that there are no genes in the Y that in any way interfere with the action of these X-borne genes.

1.	lact. ♀	×	gross. ♂	
	(gX)Y		(GX)(GX)	P.1
	(gX) Y	:	(GX)	gametes
	(GX)(gX) heterozygous		(GX)Y	F.1
	gross. ♂		gross. ♀	
	(GX) (gX)		(GX) Y	gametes

(GX)(GX) homozygous gross. ♂ | (GX)(gX) heterozygous gross. ♂ | (GX)Y gross. ♀ | (gX)Y lact. ♀ | F.2

2. lact. ♀ (gX)Y × heterozygous gross. ♂ (GX)(gX)

(gX) | Y : (GX) | (gX) gametes

(GX)(gX) homozygous gross. ♂ | (gX)(gX) heterozygous gross. ♂ | (GX)Y gross. ♀ | (gX)Y lact. ♀

3. F.1 gross. ♀ (GX)Y × lact. ♂ (gX)(gX)

(GX) | Y : (gX) gametes

(GX)(gX) heterozygous gross. ♂ | (gX)Y lact. ♀

4. As 3 above.

In the domestic fowl the phenomenon of sex-linkage—this association in inheritance of a discernible character and of the character of sex itself—has in recent years formed the basis of a large industry. Day-old chicks, every one of them guaranteed to be a female, are sold by the thousand every year. The seller does not examine their genitalia in order to determine whether the chick is a male or a female; its sex is signalled by its plumage coloration. As an example the plumage characters barred and non-barred may be cited. A non-barred (black) cock mated with barred hens produces barred male and non-barred female offspring. Sons 'take after' their mother, daughters 'after' their father, a phenomenon known as criss-cross inheritance.

The actual sex-chromosome constitution of the domestic fowl is not yet finally established, the number of chromosomes is very large and many of them are very small. Assume that it is of the Lygaeus type with female heterogamety. Assume further that the genes for the characters barred and non-barred are X-borne and that barred is dominant. A non-barred cock must then have the constitution (bx)(bx) and the barred hen (BX)Y.

Non-barred ♂		Barred ♀	
(bx)(bx)	×	(BX)Y	
(bx)	:	(BX) Y	gametes
(BX)(bx)		(bx)Y	
heterozygous barred ♂		non-barred ♀	

The day-old chick that will develop into a barred-plumaged bird has a white spot on the top of the head; those who will not be barred when adult lack this spot. The barred birds are male and can be separated from the females among day-old chicks.

The sons of this mating are barred because to be males they must possess two X-chromosomes, and because one of these must come from their barred mother who has only one to offer, one carrying the dominant barred gene. The daughters of this mating are non-barred because to be females they must receive their Y from their mother and their X from their father who has only one kind of X to offer, an X carrying the recessive gene for the non-barred character.

If the reciprocal cross is made and a barred cock is mated with non-barred hens all the F.1, males and females alike, are barred. In the F.2 there appear on the average in every 4, 3 barred and 1 non-barred. Among the barred there are two males and one female in every three and all the non-barred are females.

Barred ♂		Non-barred ♀		
(BX)(BX)	×	(bX)Y		P.1
(BX)	:	(bX)	Y	gametes
(BX)(bX)		(BX)Y		F.1
heterozygous Barred ♂		Barred ♀		
(BX)	(bX)	(BX)	Y	gametes
(BX)(BX)	(BX)(bX)	(BX)Y	(bX)Y	F.2
homozygous Barred ♂	heterozygous Barred ♂	Barred ♀	non-barred ♀	

The recessive character of the grandmother is exhibited by none of her sons or daughters and only by 50 per cent.

of her granddaughters. These facts can be explained most readily on the assumptions that the genes for the characters barred and non-barred are being distributed by a mechanism that at the same time is distributing the elements of a sex-determining mechanism and, secondly, that the male of the domestic fowl has in his constitution the sex-determining element in duplicate whilst the female possesses it in the single state and is heterogametic. Homo- and heterogamety require that there shall be a qualitative or quantitative difference of this kind between male and female.

In man there is a form of the disease haemophilia that behaves in inheritance in exactly the same way and which goes far to prove that the male is heterogametic and that haemophilia is a sex-linked recessive character, its gene being X-borne. Evans and Swezy (1929) offered cytological proof that man has the Lygaeus type of sex-chromosome constitution, the male being XY.

It will be noted that according to this explanation (on p. 22) there can be two kinds of males, haemophiliacs and normals, and three kinds of females, normals, carriers and haemophiliacs. This is so because the male has but one X-chromosome and the female two. On any one X there can be either the gene for normality or else the gene for haemophilia. In the case of the female the haemophilia gene can be present in neither, in one or in both of the X's. A male cannot be a carrier. It is because the carrier female is so difficult to identify that she constitutes a danger to her offspring by a normal male. A female can be haemophilic only when her father is a haemophiliac and her mother either a carrier or else a haemophiliac. Haemophilia is seldom encountered in the human female for the reason, it would appear, that female haemophiliacs die *in utero*.

Non-Disjunction. That the mechanism that is concerned with the distribution of these sex-linked characters is at the same time the mechanism which in its functioning is involved in the determination of the sex of the individual was proved beyond all doubt by the work of Bridges (1916) on non-disjunction in *Drosophila melanogaster*.

				Equal numbers of or equal chances of producing			
1.	normal ♂ (HX)Y	× haemophilic ♀ (hX)(hX)	=	normal (heterozygous) ♀ (HX)(hX) (carrier)	haemophilic ♂ (hX)Y		
2.	normal ♂ (HX)Y	× carrier ♀ (HX)(hX)	=	normal ♀ (HX)(HX)	carrier ♀ (HX)(hX)	normal ♂ (HX)Y	haemophilic ♂ (hX)Y
3.	haemophilic ♂ (hX)Y	× normal ♀ (HX)(HX)	=	carrier ♀ (HX)(hX)	normal ♂ (HX)Y		
4.	haemophilic ♂ (hX)Y	× carrier ♀ (HX)(hX)	=	carrier ♀ (HX)(hX)	haemophilic ♀ (hX)(hX)	normal ♂ (HX)Y	haemophilic ♂ (hX)Y
5.	haemophilic ♂ (hX)Y	× haemophilic ♀ (hX)(hX)	=	haemophilic ♀ (hX)(hX)	haemophilic ♂ (hX)Y		

The Mode of Inheritance of Haemophilia in Man

The science of genetics owes more to the fortuitous selection by T. H. Morgan and his colleagues at Columbia University in the early days of this century of *Drosophila melanogaster* as an experimental material than to any other event that has occurred during its development. It so happened that this small fly possessed every possible attribute that the geneticist could wish to find. It thrives under laboratory conditions, it multiplies rapidly and it continually threw up mutant forms at a time when the geneticist was seeking new phenotypes to explore. When the chromosome complex came to be recognized as the mechanism involved in the transmission of the hereditary characters, it was found that in respect of chromosome number Drosophila possessed but four pairs, easily distinguished one from the other and that the X and Y of the male differed markedly, so that cytologically the fly was as excellent a material as it had proved to be genetically. Then when cytological inquiry came to overtop the purely genetical in importance it was found that in the fly's salivary glands the chromosomes existed in a giant form. To a very large extent the choice of Drosophila at that time determined the rate and the direction of the development of genetics thereafter; it also affected profoundly the development of the whole range of the biological sciences to give to the Theory of the Gene an importance not less than that of Evolution Theory itself.

An early mutation in Drosophila was the recessive sex-linked white-eye character. It was quickly explained as indicated below:

Wild type red eyed ♂	×	Mutant white eyed ♀	
(WX)Y		(wX)(wX)	P.1
(WX) Y	:	(wX)	gametes
(WX)(wX)		(wX)Y	F.1
red-eyed daughters		white-eyed sons	

But to this rule there were exceptions, a number of white-eyed daughters and of red-eyed sons making their

appearance. Bridges showed that these exceptional individuals could be explained if it were assumed that the white-eyed mother was not (wX)(wX) but (wX)(wX)Y in respect of sex-chromosome constitution, if a definite abnormality in the distribution of the sex-chromosomes had occurred during the maturation of the egg from which she sprang.

Normally, of the two X-chromosomes in the unripe egg, one during the reduction division passes into the polar body. If exceptionally these X's did not so disjoin, both remaining in the egg, or if both passed into the polar body, then two further kinds of mature ova would result, one with two X's, each in this case carrying the gene for white-eye (wX), and the other without any X. The spermatozoa of the red-eyed male are of two kinds, one with an X carrying the dominant red-eye gene, the other with a Y. Fertilization of these two exceptional kinds of egg would then yield four combinations, so:

Eggs abnormal in respect of sex-chromosome constitution		Spermatozoa
(wX)(wX)	×	(WX)
(–) no X chromosome		Y
	Phenotype	Sex-chromosome constitution
1. (WX)(wX)(wX)	red-eyed female	triplo-X
2. (wX)(wX)Y	white-eyed female	XXY
3. (WX)(–)	red-eyed male	XO
4. (–)Y	?	–Y

1. Exhibits poor viability.
2. An exceptional white-eyed female. She exhibits this character because she received both of her X's from her mother.
3. An exceptional red-eyed male. He received his X from his father and not from his mother.
4. Does not appear.

The mating of a normal red-eyed male to a non-disjunctional white-eyed female (2 above) will yield the following results:

normal red-eyed ♂	×	non-disjunctional XXY white-eyed ♀	
(WX)Y		(wX)(wX)Y	
(WX) Y	:	(wX)	Four kinds of gametes, the numerical proportions of these being determined by the frequency of the different groupings of the triad components and by the variation of their positions on the spindle.
		(wX)Y	
		(wX)(wX) Y	

Fertilization	Phenotype	Sex-chromosome constitution
1. (WX)(wX)	red-eyed ♀	normal XX
2. (WX)(wX)Y	red-eyed ♀	XXY
3. (WX)(wX)(wX)	red-eyed ♀ ?	triplo-X
4. (WX)Y	red-eyed ♂	normal XY
5. (wX)Y	white-eyed ♂	normal XY
6. (wX)YY	white-eyed ♂	XYY
7. (wX)(wX)Y	white-eyed ♀	XXY
8. YY	— ?	YY

Classes 3, the trisomic red-eyed female, and 8, the double Y lacking an X, do not appear. 4, the exceptional red-eyed male, has its origin in an X from the father and a Y from the mother. 7, the exceptional white-eyed female, derives both X's from the mother. She is a female because she is XX.

The exceptional white-eyed females (7) when mated with normal red-eyed males always yield the same kind of exceptional offspring; the exceptional red-eyed males (4) always behave as normal red-eyed males, they have a perfectly normal sex-chromosome constitution even though the X and the Y are derived from the wrong parents. There are two kinds of white-eyed males (5 and 6), one perfectly normal, the other cytologically exceptional and therefore producing exceptional gametes in its turn. 6 should be able to yield an XXY female by fertilizing an X-bearing egg. It does. The XXY female has been identified both genetically and cytologically. Sex-determination would therefore seem to be an affair of the sex-chromosome combination, no

matter how this may be established. Since in these non-disjunctional types the autosomes are the same in both sexes, maleness and femaleness would seem to be characters that are based upon the number of X-chromosomes present in the zygote. It would appear from this work of Bridges that the X-chromosome itself is neither male-determining nor female-determining but is of such a kind that when one is present in association with a diploid set of autosomes development is swung in the direction of maleness, whereas when two are present it is swung in the direction of femaleness. The egg possesses the capacity to develop in either direction, the direction taken being determined by the relative amount of X-chromosome-borne chromatin.

Then in 1922 came the work of L. V. Morgan on attached X-chromosomes which finally showed that two X's in the zygote, irrespective of their origin, resulted in the production of a female. The culture of Drosophila used by L. V. Morgan exhibited a sex-linked recessive character yellow body-color. Homozygous yellow females mated to wild-type (grey body-colored) males gave only yellow daughters and grey sons, a constant and complete reversal of the expected criss-cross mode of inheritance. Cytological examination showed that in these females instead of the usual two X's there was a single V-shaped chromosome and, in addition, usually a supernumerary Y. Others possessed a single X in addition to this V. The V was shown to be two attached X's which did not disjoin during meiosis.

An attached X		Normal	
Yellow ♀		Grey ♂	
(gX)⌢(gX)Y	×	(GX)Y	
(gX)⌢(gX)		(GX)	gametes
Y		Y	gametes

	Phenotype	Sex-chromosome constitution
(1) (gX)⌢(gX)(GX)	grey female	triplo-X
(2) (gX)⌢(gX)Y	yellow female	XXY
(3) (GX)Y	grey male	XY
(4) YY	?	YY

G=the gene for grey body-colour; g=yellow; ⌢=attached.
(1) rarely survives. (4) is non-viable and does not appear.

Thus the addition of a Y to XX has no discernible effect upon the sex-differentiation of the individual. The X-bearing sperm which usually takes part in the creation of a female here contributes to the origin of a male if it fertilizes a Y-bearing egg. Sex is thus determined by the sex-chromosome distributing mechanism which operates at the time of karyogamy.

It is now established that the Y-chromosome is not completely inert. Part of it is inert but there is a portion which carries genes and which is homologous gene by gene with the X-chromosome. Both Bridges and Stern (1927) have identified 'fertility' genes in the Y and Sturtevant showed that the reason why the males of a 'bobbed' stock do not exhibit this recessive sex-linked character is that there is a dominant normal gene in the Y.

Gynandromorphism. The essential feature of the condition of gynandromorphism is the presence in one and the same individual of a species in which sex-dimorphism is the rule, of sharply defined regions of the body some of which show the characters of the male, others of which display the characters typical of the female. A gynandromorph is a sex-mosaic in space. A 'lateral' gynandromorph has one half of the body, the left or the right, including the reproductive organs, completely male in its characterization while the other half displays the typical female characterization; in an anterior–posterior gynandromorph the anterior half of the body has the characterization of one of the sexes, the posterior half those of the opposite sex. The sex-mosaic can be much less regular than this, however, most of the regions of the body displaying the characters of one sex and only a relatively small area exhibiting those of the other.

Time came when this phenomenon of gynandromorphism could with great advantage be investigated in *Drosophila melanogaster*. The genetic and cytological analysis of this fly came to be very advanced. The spacial relationships in the different chromosomes, both autosomes and sex-chromosomes, of several hundreds of genes were quickly

determined by planned experimentation. Gynandromorphism is not uncommonly encountered in this form.

Morgan and Bridges (1919) showed that in these *Drosophila melanogaster* gynandromorphs whereas the transmission of the autosomal characters was not affected, both male and female parts displaying them equally, that of the characters the genes for which were X-chromosome-borne was disturbed. It was possible therefore to conclude that in such a gynandromorph the male and female regions differed from each other in respect of the X-chromosome content of the nuclei of their component cells.

A lateral gynandromorph with a white-eyed side displaying the male characterization and a red-eyed side exhibiting the female characterization can be explained as follows:

White eyed ♂	×	Red eyed ♀	Parents
(wX)Y		(WX)(WX)	
	(WX)(wX)		the gynandromorph in its beginning

The gynandromorph started its life as an XX individual, being the result of the fertilization of an egg with an X-chromosome carrying the dominant gene for red-eye by a spermatazoon with an X-chromosome carrying the recessive gene for the white-eye character. At the first division of this fertilized egg when each of these X's splits longitudinally and when normally each of the nuclei of the two resulting daughter cells receives two daughter X's, one paternal and one maternal in origin, one of these daughter X's—the maternal one carrying the dominant red-eye gene —became excluded from one of the daughter nuclei. The sex-chromosome constitution of the two daughter nuclei therefore came to be:

(wX) : (WX)(wX)

Then if from each of these cells there arose the tissues of one lateral half of the body and if the single X constitution equals maleness and the XX constitution leads to the development of femaleness, a 'half sider' should result, one side being male and white-eyed, the other female and red-eyed.

If this explanation is valid, then gynandromorphism in *Drosophila melanogaster* is the result of the elimination of an X-chromosome from the nucleus of one of the cells produced by the first cleavage division of a female zygote (XX). XO tissue is male tissue. If such elimination occurs at the second cleavage division a quarter of the body becomes XO in constitution and male in characterization. The later in embryonic development this elimination occurs the less will be the amount of male tissue in such an individual. When in an elimination gynandromorph the abdomen is affected and is male-type, the individual behaves as a male but is invariably sterile.

Morgan and Bridges (1919) found in a series of about a hundred that the maternal X was eliminated about as frequently as was the paternal.

Doncaster (1914) noted that in the moth Abraxas there was occasionally to be encountered an egg with two separate maturation spindles and two female pronuclei each about to be fertilized by a separate sperm. If each of these pronuclei was fertilized by a separate spermatozoon, and if one of these was X-chromosome-bearing, the other Y-chromosome-bearing, such double fertilization could yield a gynandromorph. Bridges (Morgan, Bridges and Sturtevant, 1925) came across such a dizygotic gynandromorph in *Drosophila melanogaster* in a back cross involving the recessive characters speck and vestigial, the genes for which are resident in the second chromosome. The right side of the body was predominantly female and displayed the character speck; the left side was mostly male and exhibited the vestigial wing character. The ovum had two nuclei, in each of which was an X and a 2nd chromosome. One of these nuclei united with a sperm carrying an X and a 2nd, the other with a sperm with a Y and a 2nd. From each of these fertilized nuclei one side of the body developed.

	Egg nucleus	Sperm
Right side	X 2nd speck	X 2nd vestigial speck
Left side	X vestigial	Y vestigial speck

Only rarely was it found that these dizygotic mosaics differed laterally in respect of the sex-characters.

CHAPTER 4

SEX-DETERMINATION IN HABROBRACON, SCIARA AND *LYMANTRIA DISPAR*

Habrobracon. As long ago as 1845 Dzierzon observed that in the honey-bee the sex of the individual was determined by the occurrence or non-occurrence of fertilization; the egg being fertilized gave rise to a female; the egg not being fertilized and developing parthenogenetically yielded a male. This difference was later interpreted as a difference between diploidy (in respect of the chromosomes) and haploidy and was found to be characteristic of the hymenoptera generally. The possible evolutionary origin of this haplo-diploid sex determining mechanism has been reviewed by White (1945) and Whiting (1945).

When Bridges formulated his concept of genic balance it became necessary to discover whether or not the facts relating to parthenogenesis could be newly interpreted. According to this concept the haploid stated yielded maleness as did also this state in duplicate. If diploidy was to yield femaleness, then the two sets of chromosomes had to be qualitatively different so that where 1N=maleness, N+N′=femaleness.

That this is so has been shown by Whiting and his school working with the wasp *Habrobracon juglandis* which is parasitic on larvae of the meal moth Ephestia. Torvik-Greb (1935) showed that in Habrobracon the female is diploid with 20 chromosomes and the male haploid with 10. The reduced egg has a set of 10 and the sperm, through an aborted reduction, retains 10. Fertilized eggs have 10+10 and give rise to females; the same eggs unfertilized develop parthenogenetically into males with a set of 10 maternal chromosomes.

These cytological findings are in harmony with the sex-linked mode of inheritance displayed by certain mutant forms. Thus when a female with the recessive mutant orange

eye-colour is mated with a wild-type male (black eye-colour) the daughters are black-eyed and the sons orange-eyed.

But it was found that in matings in which the orange-eyed mother and the black-eyed father were from the same stock or from stocks closely related through inbreeding, black-eyed sons appeared. By genetical experiment and by cytological examination these were shown to have received a chromosome set from both the father and the mother, having 20 altogether and being heterozygotes.

The hypothesis elaborated to account for these 'biparental males' rests on the assumption that the normal female is a heterozygote in respect of two sets of multiple sex alleles or differential chromosome segments which for purposes of discussion may be designated X^a and X^b respectively. There are two kinds of the normal haploid male, X^a and X^b. The 'biparental male' is $2X^a{:}2A$ or $2X^b{:}2A$, with the same genic balance as the ordinary haploid male $X^a{:}A$ or $X^b{:}A$. The normal diploid heterozygous female is $X^a{:}A/X^b{:}A$. So that the male is N^a or N^b, the female N^a/N^b, and the 'biparental male' N^a/N^a or N^b/N^b.

The fact that inbreeding yielded a marked increase in the production of 'biparental males' resisted satisfactory explanation for a long time (Bostian, 1934; Whiting, 1935; Snell, 1935). Ultimately Dordick (1937) was able to show by a number of ingenious experiments that the low incidence of biparental males (1 such to 9 biparental females in the ordinary laboratory stocks) was due to the conversion by gene action of the biparental male into a female, the gene or genes concerned being resident not in the X but in another chromosome, the so-called Z. Thus in Habrobracon the existence of multiple sex-differentials in different chromosomes was disclosed and the notion of genic balance shown to apply.

Dreyfus and Breuer (1944) found in another parasitic wasp *Telenomus fariai* a special chromosome mechanism which makes inbreeding compatible with a method of sex-determination resembling that in Habrobracon.

In the Iceryini the sex-determining mechanism is of the

haplo-diploid type. The genic balance concept of sex-determination cannot be applied since the ratio of male-determining to female-determining genes is the same both in the haploid male and the diploid female. Formal explanation is possible by means of the hypotheses advanced by Goldschmidt (1920) and by Schrader and Sturtevant (1923). The former suggests that precocious activity by the male-determining genes in the diploid dose and prior to reduction predispose all eggs to a male pattern of sexual differentiation and that this is then overridden in fertilized eggs by the delayed activity of two sets of female-determining genes. But this 'turning-point' hypotheses is not generally accepted. The algebraic sum hypothesis of Schrader and Sturtevant, helpful and ingenious as it is, is not suitable for general application.

Sciara. Metz (1938) and his colleagues studied the genetic and cytological aspects of sex-determination in the dipteran fungus-gnat *Sciara coprophila* over a long period of years and have recorded much that is remarkable. A given female produces offspring predominantly of one sex. Among the families in which most of the progeny are females there are two types of females, female-producers and male-producers, indistinguishable on inspection and in respect of the behaviour of their chromosomes. They differ genetically, however. The female-producers may be designated XX^1, being heterozygous for a gene in the X, and the male-producers as XX, being homozygous for the recessive allele of this gene. Males are genetically XO:AA in somatic constitution and produce one type of sperm, XXA. A given female produces the same kind of offspring, whether sons or daughters, irrespective of the origin of the male to which she is mated.

The mode of inheritance of certain mutant characters is peculiar. Metz (1927) used an autosomal recessive mutant truncate wing. Truncate ♀ × wild-type ♂ gave none but wild-type. Some of the F_1 families were mostly daughters, others mostly sons. F.1 ♂ × homozygous truncate ♀ gave all truncate, daughters in some families, sons in others. But

when truncate male was mated to a wild-type female and the F.1 wild-type males back-crossed to truncate females, all the offspring were wild-type. The male had transmitted to his offspring only that allele which he had received from his mother. This matroclinous inheritance manifestly differs from sex-linked inheritance for the character truncate is distributed alike to both males and females.

Metz and Schmuck (1929), using a sex-linked recessive mutant swollen wing, found that swollen ♂ × wild-type ♀ gave all wild-type in F.1 and that in F.2 swollen reappeared in half the sons in the male families but in none of the daughters of the female families. Swollen ♀ × wild-type ♂ gave swollen sons, the swollen females all proving to be male-producers. Thus the mutation had occurred in the X and had not passed into the X^1 through crossing-over.

A dominant mutant gene 'Wavy' was found by Metz and Smith (1931) to have occurred in the X^1 and not to have crossed over into the X.

Thus it would seem that female-family-production is a character determined by a dominant gene in the X chromosome (X^1) and that male-family-production is a character based on the recessive allele of this gene.

The reason for this matroclinous inheritance—the male transmitting to his progeny only those genes, sex-linked and autosomal, that he himself received from his mother, his spermatozoa lacking the paternal chromosomes—has been revealed by cytological investigation (Du Bois, 1932). Femaleness in Sciara is determined by the genic balance, 2X:2A=femaleness; 1X:2A=maleness. The dominant gene (X^1) acts by so conditioning the cytoplasm that in the X^1X:2A constitution one paternal X is eliminated from the nucleus. The XX:AA constitution leads to the elimination of two paternal X's and to the soma of the male becoming XO:AA.

Lymantria dispar. The term intersex was first used by Goldschmidt in 1925 to describe certain sexually aberrant types that he had described in 1911 and which had appeared

among the offspring of the mating of European Lymantria females and Japanese Lymantria males. This mating gave normal sons and individuals showing a mixture of male, female and intermediate characters.

It has long been known to entomologists that crosses between different geographical varieties of the Gypsy moth sometimes yield these sexually aberrant forms. This intersexuality is in no way associated with any corresponding abnormality in respect of chromosome number or behaviour. The female is the heterogametic sex. Goldschmidt (1920, 1931, 1934) was able to classify the intersexes according to their characterizations into two main types, male intersex and female intersex, the former being an XX individual which exhibits female as well as male characters, the latter an XY individual with both female and male characters. The intersex is a sex mosaic. The female intersexes range from the unexceptional female, through increasing grades of intersexuality—i.e. with increasing degrees of maleness—to complete sex-reversal—i.e. an XY individual that is a functional male. A corresponding series of male intersexes ranges from complete maleness to complete femaleness.

A careful examination of great numbers of intersexual individuals permitted Goldschmidt to conclude that there was indeed a time seriation of events in the development of the sex-characters—that is to say, that all the structures of the sex equipment were not differentiated at any one time but that one structure of this equipment appeared before another, and so on, and that the grade of intersexuality was determined by the relative number of these structures that were male and female in type respectively. It appeared that the last structure of the sex-equipment to become differentiated in the life history of the individual was the structure most commonly affected in this process of intersexuality, and that a greater number of these structures became affected with each increasing grade of intersexuality.

The original matings on the results of which Goldschmidt's hypothesis is founded were as follows:

European ♀ × Japanese ♂=F.1: all sons normal, all daughters intersexual
F.2: all sons normal, half daughters normal, half intersexual (the grade of intersexuality being as that in the mother. Only the lower-grade intersexuals could be bred from)

Japanese ♀ × European ♂=F.1: sons and daughters all normal
F.2: all daughters normal, half sons normal, half intersexual

For purposes of description and discussion Goldschmidt refers to the Japanese race in these experiments as a 'strong' race, and the European as 'weak'. Female intersexuality is produced in an F.1 when a 'weak' female is crossed with a 'strong' male. Male intersexuality is exhibited by a proportion of males in the F.2 of the cross 'strong' female × 'weak' male. From these results it is seen that sex-determination is a phenomenon partaking of the nature of a genic balance, sex being dependent upon a particular relation of certain determiners, their relative 'strength' or 'weakness'; in other words, a balance or lack of balance of these determiners. It is clear that these determiners are of two kinds, one of which shifts sex toward the female type, the other toward the male.

In order to determine how these sex-determining factors were transmitted, Goldschmidt carried out the following breeding experiments:

A. F.1 weak ♀ × strong ♂ gave ♂♂ all normal and ♀♀ intersexual
F.2 weak ♀ × strong ♂ gave ♂♂ all normal; ♀♀ half normal, half intersexual
Backcross. Weak ♀ × F.1 (weak ♀ × strong ♂) ♂ gave ♂♂ normal; ♀♀ half normal, half intersexual
Backcross. Weak ♀ × F.1 (strong ♀ × weak ♂) ♂ gave ♂♂ normal; ♀♀ half normal, half intersexual
Backcross. F.1 (weak ♀ × strong ♂) ♀ × weak ♂ gave ♂♂ all normal; ♀♀ all normal
Backcross. F.1 (weak ♀ × strong ♂) ♀ × strong ♂ gave ♂♂ all normal; ♀♀ all intersexual

In all these crosses it is the maternal line that is 'weak'. The results show at once that the 'strength' which produces

female intersexuality is transmitted in the X-chromosomes, and the results are exactly what would be expected if this intersexuality-producing 'strength' is a property of the X-chromosome of the 'strong' race. They show, further, that the X-chromosome of the 'weak' race carries the determiner of this property 'weakness', and, finally, they show that the F.1 females behave like pure 'weak' females.

B. F.1 strong ♀ × weak ♂ gave ♀♀ all normal; ♂♂ all normal
F.2 strong ♀ × weak ♂ gave ♀♀ all normal; ♂♂ half normal, half intersexual
Backcross. Strong ♀ × F.1 (strong ♀ × weak ♂) ♂ gave ♀♀ all normal; ♂♂ all normal
Backcross. Strong ♀ × F.1 (weak ♀ × strong ♂) ♂ gave ♀♀ all normal; ♂♂ all normal
Backcross. F.1 (strong ♀ × weak ♂) ♀ × strong ♂ gave ♀♀ all normal; ♂♂ all normal
Backcross. F.1 (strong ♀ × weak ♂) ♀ × weak ♂ gave ♀♀ all normal; ♂♂ all intersexual

These results show that the property 'weakness' (weak males) is transmitted in their X-chromosomes, that in these combinations two 'strong' X-chromosomes or one 'strong' and one 'weak' produce normal males, two 'weak' X-chromosomes produce intersexual males, and that all the mothers in this series behave as 'strong' females whether they belong to a pure strong race or whether they be hybrids out of a 'strong' mother and a 'weak' father.

If the two lots of results are considered together it is seen that 'strength' and 'weakness' are, firstly, characters, the determiners of which are carried in the X-chromosomes of the respective races, and, secondly, that 'strength' and 'weakness' are properties which are inherited only in the female line. Sex is determined by a definite relation or balance between the respective 'strength' or 'weakness' of one type of sex-determining factors inherited maternally and the other type which are transmitted within the X-chromosomes. It is seen, further, that the combination of the 'weak' maternally inherited determiner with a 'strong' X-borne determiner shifts the female (XY) toward maleness, whereas the combination of a 'strong' maternally

inherited determiner with two 'weak' X-borne determiners shifts the male (XX) toward femaleness. It follows, therefore, that the X-chromosomes must contain male-determining factors, 'strong' in the 'strong' and 'weak' in the 'weak' races, and that the female-determiner also 'strong' in the 'strong' and 'weak' in the 'weak' races, is not to be found in the X-chromosome but elsewhere. Goldschmidt has adduced reasons for the view that the female-determining factor is resident in the Y-chromosome. Thus sex in the Gypsy moth, he suggests, is determined by a relational balance between a maternally inherited (Y-borne) female-determiner (F) and a male-determiner (M), of which one is present in the female and two in the male, and which is borne in the X-chromosome. Intersexes appear if in a hybrid combination of M and F these sex-determining factors are not properly balanced. Goldschmidt regards the M and the F as being single genes for the reason that never in thousands of crosses has any result been obtained which would support any other conclusion.

His results can be illustrated in simple fashion by the following scheme: In the Gypsy moth the male has a sex-chromosome constitution XX, while the female is XY. The male-determining genes are resident in the X-chromosomes, the female are in the Y and are therefore restricted to the maternal line. But Goldschmidt gained evidence which forced him to the conclusion that the female-determining factors borne on the Y-chromosome acted prezygotically—that is to say, before the X and the Y chromosomes in the naturing egg had separated. The physiological effects of the action of these Y-borne genes would thus pervade the whole of the immature egg. Two kinds of eggs would be produced, an X-bearing egg, the Y-chromosome having passed into the polar body, or a Y-bearing egg, the X-chromosome having passed into the polar body, but, in respect of the female-determining reactions which result from the functioning of the Y-borne gene, the X-bearing egg and the Y-bearing egg produced by the same female are exactly alike.

A male like a female has its origin in an egg, but in the

union of an X-bearing sperm with an X-bearing egg. Since this egg is already endowed with female-determining properties of a certain valency, the symbol for male must be (MX)(MX)F whilst that for a female is (MX)F. In order to simplify the symbols it is convenient to leave out the X and to indicate a male by the formula MMF and a female by MmF (the small m indicating that only one X chromosome is present). The female-producing tendency of the cytoplasm F can be overcome by MM but not by M, and so in each generation equal numbers of normal males and females are produced in the case of each pure race of Lymantria. The explanation of the appearance of intersexes on crossing different races turns upon the assumption that the intensity of the action of M and F differs in different races. The M and F in *L. japonica* are stronger, and exert their influence earlier in the course of development, than the M and F of *L. dispar*.

The relative 'strength' and 'weakness' of the sex-determining genes can be indicated by assigning to the M and F numerical values, e.g. M_5 is much stronger than M_3, and M_3 than M_1. F_1 is much weaker than F_3, and F_3 weaker than F_5. Now, consider the mating of a 'weak' female (M_2mF_3) to a 'strong' male ($M_5M_4F_4$). (It will be noted that the male-determining factors of the male have a different valency. This is possible since the two X-chromosomes which carry these come from different parents which may differ in respect of the valency of their sex-determining factors.) The female will elaborate two kinds of eggs—one M_2F_3 and the other mF_3. The male will elaborate two kinds of sperm—M_5 and M_4. It is to be noted that the female-determining factors are restricted entirely to the female line. These four kinds of gametes, two from each side, will provide the following types in the F_1: $M_5M_2F_3$; M_5mF_3; $M_4M_2F_3$; M_4mF_3.

Now, sex is determined by that kind of sex-determining reaction which is in effective excess. In the case of the $M_5M_2F_3$, M=7, F=3—that is, M is greater than F. The sex-chromosome constitution is XX and therefore this individual is a normal male. In the case of the class M_5mF_3,

M is greater than F, so that in spite of the fact that this individual is XY in sex-chromosome constitution, that is, genetically a female, it will be intersexual; in fact, according to the argument it will be a genetical female completely transformed into, and functioning as, a male. Individuals $M_4M_2F_3$ are normal males, whilst those which are M_4mF_3 are genetically females, but nevertheless are females transformed into males.

A survey of the Central European and Japanese races of Lymantria has provided Goldschmidt with different strains which possess all kinds of combinations of 'strong' and 'weak' male-determining factors, with 'weak' and 'strong' female-determining factors, and by the use of them he was able to produce any percentage of intersexual forms and any grade of intersexuality, either male or female, at will. Whilst in Japan Goldschmidt was enabled to distinguish eight different strains of Lymantria, and an elaborate series of breeding experiments permitted him to arrange them in a series of decreasing strength. The differences between the extremes of this series were greater than those between the European *dispar* and the *L. japonica* which he first used. Indeed, it was so great that when a 'strongest' father was mated with a 'weakest' mother, the progeny consisted solely of males, half of these being chromosomally males M_8M_8F, whilst the rest were really females M_8mF in which the male-determining factor, introduced from the strong race, had overwhelmed the female-determining factor of the weaker. The 'strength' or 'valency' of the sex factors differed for each race; but in each race it was fixed. Goldschmidt holds the view that this fixity is really quantitative, depending upon definite amounts of the sex-determining material present in any case. He has satisfied himself that the different degrees of strength and weakness of these sex-determining factors reveal the existence of a series of multiple allelomorphs, but, more recently, he has been forced to the conclusion that in the case of the mating 'strong' Japanese × 'weak' European a pair of autosomal allelomorphic modifying genes is involved which affects the expression of male intersexuality. Goldschmidt's results show that the different

conditions of the male- and the female-determining factors of the different races form an orderly quantitative series in regard to their effect and that different possible combinations behave exactly as if the different degrees of strength of these genes could be expressed in numerical values.

The genetical basis of sex and intersexuality as understood by Goldschmidt is given by the amount of balance or imbalance between M and F at the beginning of development. In the uneventful differentiation of the normal male M is always effectively in excess of F; in the case of the normal female F is at all times effectively in excess of M, but in the development of the intersex the relationship of M and F is disturbed; M (or F) overtakes and replaces F (or M) at some point—the turning-point or switchover. The effect of this genic situation is that at a certain moment in development the switch-over occurs and the control of the remaining events in sexual differentiation is shifted from the F to the M genes, or vice versa, and the time of occurrence of this event is the simple function of the relative degree of balance or imbalance between F and M. It would seem that M and F respectively are responsible for sex-determining reactions which proceed with a velocity proportional to the strength or valency or quantity of these genes; that the quicker reaction controls the sexual differentiation and that the two curves of M and F reactions may have points of intersection, that is, at the switch-over, if the quantities of M and F are not properly matched. If this is so, then it should be possible to produce abnormal forms by changing the relative velocities of these two reactions within a pure normal race, through the differential action of temperature, for example. This Goldschmidt has done with positive results, producing intersexuality by the action of extreme temperature within a pure race.

Winge (1937) offered an alternative explanation of the observations that required Goldschmidt to postulate cytoplasmic inheritance. He suggested that the X-chromosome contains a preponderance of male-determining genes, strong (M 50) in the Japanese variety and weak (M 10) in the European; that the Y has a preponderance of female-

determining genes, very strong (F 70) in the Japanese variety and weak (F 24) in the European; that all the autosomes carry sex-determining genes, some male- and some female-determining, and that in the Japanese variety the autosomal female-determining genes are strong (F 20) and weak in the European (F 4).

By the use of these assumptions, which are exactly like those made by Goldschmidt himself elsewhere, all reference to the cytoplasm can be avoided and the facts of sex-determination in Lymantria can be brought into line with the rest.

Baltzer (1937), who for many years had been studying problems of sex-determination and of intersexuality in *Bonellia viridis*, found himself unable to accept Goldschmidt's notion of the turning point or switch-over.

This marine worm in its larval form floats on the surface of the sea. When it settles on or near the proboscis of an adult female it thereafter pursues a male differentiation. If, on the other hand, chance leaves it far removed from an adult female, it becomes a female. If the young individual, having begun to differentiate as a male, is removed to a distance from the adult female its differentiation switches to the female pattern and an intersexual form results. It has been shown that there is a chemical substance in the female's proboscis which dominates the sexual differentiation of the young individual.

These events relate to the physiology of sex-differentiation and not to the phenomenon of sex-determination. There may or may not be a chromosomal, genetic, sex-determining mechanism in Bonellia. If there is it is overridden by an external chemical influence.

Baltzer is satisfied that in the intersex of Bonellia there is no purely male development period followed by a female development period but that the intersexual organs are intersexual from the beginning.

CHAPTER 5

GENITIC INTERSEXUALITY IN DROSOPHILA, CERTAIN LEPIDOPTERA AND BIRDS

Drosophila. The first description of a gene in Drosophila which profoundly affected the sexual characterization was that given by Sturtevant (1920) in *D. simulans*. In a particular stock it was noted that many individuals exhibiting a definite intersexual condition appeared. They were sterile, but the mating of their apparently normal brothers and sisters to unrelated stocks commonly produced the same abnormal forms in the F_2 generation, the sex-ratio being of the order of 4 males; 3 females, 1 intersex, which suggested that these intersexes were modified females. By the use of sex-linked genes Sturtevant was able to demonstrate that this was so, and further breeding experiments showed that the agent responsible was a recessive gene resident in the second chromosome.

In *Drosophila virilis* Lebedeff (1934) found a third chromosome recessive gene which transformed the XX individual into a sterile male but left the XY individual unaffected. Later (1937) Lebedeff showed that the XX individual began its development according to the female pattern and that later male organs made their appearance, the two sets, male and female, continuing thereafter to develop side by side.

Bridges (1921, 1922, 1925) described a form of intersexuality in *Drosophila melanogaster* caused by an altered ratio of sex-chromosomes and autosomes. These intersexes showed complex mixtures of male and female parts. They could be produced by breeding from certain of their sisters which were to be distinguished by their large coarse eyes, thick-set bodies, coarse bristles and hair pattern on the wing. Cytological examination demonstrated that these intersex-producers were triploids, every chromosome being present in triplicate (3N). All the eggs produced by them

contained one full set of chromosomes and part or all of an extra set. The diploid (2N) eggs fertilized by X-sperm gave rise to 3N females; fertilized by Y-sperm they gave the intersexes which were 2X:3A as contrasted with the 2X:2A normal female (X=X chromosome; A=one haploid set of autosomes).

These observations made it clear that sex was determined not, as had been thought, by the presence of one X or two, but by the balance between the X and the autosome material, by the genic balance. Dobzhansky and Bridges (1928) carried this work to its conclusion to find that X>A, i.e. that the net male-determining tendency of a set of autosomes is less than the next female-determining tendency of an X.

1X:2A=a male
2X:2A=a female

If the female-determining tendency of the sex-determining genes in an X-chromosome is represented by the figure 100, then the net male-determining tendency of the sex-determining genes in a set of autosomes is of the order of 80.

1X:2A
100 160
2X:2A
200 160

The following abnormal types could be expected and were to be explained as under:

Sex-type	Formula	X=100	A=80	Sex-index
Superfemale	2N 3X:2A	300	160	1·88
Female	4N 4X:4A	400	320	1·25
	3N 3X:3A	300	240	1·25
	2N 2X:2A	200	160	1·25
	1N 1X:1A	100	80	1·25
Intersex	4N 3X:4A	300	320	0·94
	3N 2X:3A	200	240	0·83
Male	2N 1X:2A	100	160	0·63
	4N 2X:4A	200	320	0·63
Supermale	3N 1X:3A	100	240	0·42

Most of these sex-types have been encountered and have been found to conform with the predictions made.

Sex-determination would therefore seem to be the end result of a quantitative balance between X-chromosomes and autosomes. In *Drosophila melanogaster* the X is not a determiner of sex but is a differential. The genes that are concerned in sex-determination are scattered irregularly throughout all the chromosomes, sex-chromosomes and autosomes alike. In a general way these genes are to be classified as female- and male-determining and the two types are in a way opposed to each other. In the X the genes for femaleness preponderate over those for maleness so that this chromosome is, on the whole, female-determining. In the second and third chromosomes the male-determining genes preponderate over the female-determining genes and these chromosomes therefore are on the whole male-determining. The fourth chromosome is mainly female-determining.

'Both sexes are due to the simultaneous action of two opposed sets of genes, one set tending to produce the characters called female and the other to produce the characters called male. These two sets of genes are not equally effective, for in the complement as a whole the female-tendency genes outweigh the male-tendency genes, and the diploid (or triploid) form is a female. When the relative number of the female-tendency genes is lowered by the absence of one X, the male-tendency genes outweigh the female, and the result is the normal haplo-X male. When the two sets of genes are acting in a ratio between these two extremes, as in the ratio of 2X:3 sets of autosomes, the result is a sex-intermediate—the intersex.'

The use of fragments of the X-duplications of various lengths and from different regions of the chromosome and of deficiencies of the X by Dobzhansky and Schultz (1934) provided experimental proof of these assumptions.

Lepidoptera. Standfuss (1908) crossed *Saturnia pyri* and *S. pavonia* and then back-crossed the F.1 males to *S. pyri* females to get 42 males and 38 'gynandromorphs'. Federley

(1913) mated *Pygaera anachoraeta* females with *P. curtula* males and back-crossed the F.1 males to *P. anachoraeta* females to get similar 'gynandromorphs'. He then examined his material cytologically to find that the haploid number for *P. anachoraeta* is 30 and for *P. curtula* 29. In the spermatogenesis of the F.1 males all 59 chromosomes divided equationally so that the 'gynandromorphs' received 59 chromosomes from their hybrid father and 30 from their mother. They were triploids 2X:3A (possibly +Y).

Seiler (1937) obtained similar triploid intersexes in the F.1 of the mating of females of the tetraploid (4N=120) parthenogenetic variety of *Solenobia triquetrella* with males of the diploid (2n=60) bisexual Nürnberg variety of the same species. The intersexes had 90 chromosomes and showed a mixture of male and female parts of varying degrees of development. Seiler found no support in his material for Goldschmidt's 'turning point' hypothesis.

Birds. That sex-determination in the fowl is likewise a matter of a quantitative balance between sex- and autosomes was strongly suggested by Crew and Munro's (1938, 1939) studies of gynandromorphism and lateral asymmetry in birds. Several instances of lateral gynandromorphism in the fowl have been reported. In such the size difference between the two sides of the body can be of the order of 10–15 per cent. and the gonads are different, one being a testis the other an ovary or ovo-testis. The explanation offered was that non-disjunction of an autosome had occurred to result in bilateral heteroploidy, there being the gain of an autosome on the larger side, its loss on the smaller, and that this disturbance of the quantitative balance between sex- and auto-somes was responsible for the gonadic differences.

CHAPTER 6

SEX-DETERMINATION IN FISH AND THE LOWER ALGAE SEX IN PARAMECIUM AND FUNGI SEX-DETERMINATION IN BRYOPHYTES SEX IN THE HIGHER PLANTS

Fish. The identification of the sex-chromosomes in fishes is difficult, but the evidence derived from genetic experimentation with Lebistes, Aplocheilus and Platypoecilus has shown that in some species the male is the heterogametic sex and that in others he is homogametic.

Winge (1922, 1934) has produced convincing evidence that in *Lebistes reticulatus* there are several mutant genes in the Y-chromosome. Spot, a large black spot on the dorsal fin, is a character exhibited by a certain geographical variety of this fish. Spot ♂ × ♀ of a variety lacking this spot=F.1 and F.2 spot males. Non-spot ♂ × ♀ of a spot variety=F.1 and F.2 non-spot males. The character of the father is transmitted to all his male descendants. Winge explained this by postulating that the male was XY and that the spot gene was Y borne.

Since then Winge has described eight other characters that in inheritance behaved like spot. He has also described eight other recessive characters, patterns of male coloration, the genes for which are presumably resident in the X for the characters were not exhibited by the F.1 but reappeared in 50 per cent. of the males in F.2. Occasionally, however, an F.1 male exhibited the character. Winge explained this by postulating that the X was homologous to a portion of the Y and that crossing-over had occurred between these homologous parts. When such an exceptional F.1 male was used in breeding, all his sons displayed the character.

In two varieties Winge observed a marked inherited tendency toward the production of females with male-like gonopodia and remarkable in that in them the heterozygous

characters with genes in the X showed up faintly. He interbred these varieties and obtained a small proportion of XX individuals (according to the genetical evidence) that were males in appearance, behaviour and function.

When these XX males were mated all of their progeny turned out to be females. The father mated to his daughters gave none but females. Mated to some of these new daughters he produced a completely male individual among the progeny. When this new male was mated with his sisters about half of the offspring were males.

In this way Winge produced a new kind of male, XX instead of XY. The X was no longer the sex-differential and the characters based on X-borne genes were exhibited by both sexes, behaving as characters based on autosomal-borne genes. The new fish was XX male; XY female; but the sex-differential function had been assumed by an autosome through the accumulation in it of male-determining genes.

It now became possible for Winge to produce YY sons who inherited the Y-borne characters from both father and mother.

Winge concludes that male-determining and female-determining genes are scattered throughout the autosomes and sex-chromosomes alike and that sex-determination is the outcome of the specific balance between the two kinds.

Aida (1921, 1930, 1936), working with the Japanese Killifish *Aplocheilus latipes*, obtained results completely parallel with those of Winge and offered a similar interpretation.

The genetical evidence relating to the Mexican Killifish *Platypoecilus maculatus* and obtained by Bellamy (1928) pointed directly to the conclusion that in this species, in contrast to Lebistes, the female is the heterogametic sex and that crossing-over occurred between the X and the Y. In two broods Chavin and Gordon (1951) obtained none but males. The female parents were XX, the male YY, so that all the offspring were XY, which is characteristic of the normal male in this strain.

Lower Algae. Hartmann and his colleagues (1932) have shown that different strains of the unicellular *Chlamydomonas eugametos* can be classified into two groups, designated plus and minus. Plus cells never unite with plus and minus never unite with minus. In certain conditions a plus cell fuses with a minus cell to form a diploid zygote. This undergoes two meiotic divisions and gives rise to 4 haploid zoospores, two of which belong to the plus and two to the minus types. They behave therefore as though they were different and contrasted sexual forms.

Paramecium. Sonneborn (1947) and others have shown that several species of Paramecium and one species of Euplotes are divisible into mating types between which, but not within which, conjugation takes place. Within a species there can be anything up to eight of these mating types. If, therefore, these mating types are regarded as sexual types they provide examples of the phenomenon of multiple sexuality which is encountered also among the algae and fungi.

Fungi. Blakeslee (1904) showed that in the bread mould Mucor zygospores are sometimes formed by the union of hyphae from the same mycelium, being homothallic, but that in most instances zygospores are formed only when two distinct mycelia come together, these mycelia being sexually different or heterothallic. Within a given heterothallic species every individual can be assigned to one of two types plus and minus. Two plus individuals will not unite sexually, neither will two minus individuals. It is when plus and minus mycelia come in contact that zygospores are produced.

Bryophytes. In most of the bryophytes the gametophytes are haploids, being of two kinds, one female (XA) and the other male (YA). In 1917 Allen described the large X and the small Y of *Sphaerocarpus donnellii* in which the haploid female gametophyte has seven autosomes and a very large X, the male gametophyte seven autosomes and a very

small Y. Since then (Allen, 1936) some thirty other bryophytes have been shown to have distinguishable sex-chromosomes.

Mackay and Allen (1936) have found X:2A and 2X:2A female gametophytes and 2Y:2A male gametophytes in Sphaerocarpus. But gametophytes with the constitution XY:2A were found to be intersexes. Similar polyploids described by Knapp (1936) indicated that the male-determining genes preponderate in the autosomes and that the Y was neutral.

The Higher Plants. Sex-chromosomes have been discovered also in the angiosperms. Santos (1923) found 24 matched pairs of chromosomes in the female and 23 matched pairs and an unequal XY pair in the male of the dioecious *Elodea gigantea*. Since then some fifty dioecious angiosperms have been shown to have distinguishable sex-chromosomes and in some twenty other dioecious species no such discernible difference could be detected. It would appear that, as a rule, in these dioecious species the male is the heterogametic sex. Only in one of them was the female the heterogametic sex and only in one, *Dioscorea sinuata*, was the male found to be XO.

Sex-linkage has been encountered in Melandrium (Baur, 1912; Shull, 1914). In this form Winge (1923) found a visibly distinct XY pair of sex-chromosomes in the male, the female being XX. Other sex-linked characters in Melandrium have been described by Winge (1931), who showed that crossing-over between the X and the Y occurred.

The monoecious (haemophroditic) *Bryonia alba* is closely related to the dioecious (bisexual) *B. dioica*. Correns (1907) found that the cross *B. dioica* ♀ by the pollen of *B. alba* gave only females, occasionally with a few male flowers. The reciprocal cross *B. dioica* ♂ × *B. alba* pistillate flowers gave females (with an occasional male flower) and males in equal numbers.

There are no visibly distinguishable sex-chromosomes in either of these species (Meurman, 1925). The hybrid progeny are all sterile.

These results can be explained on the following assumptions: (*a*) 2X:2A=♀ XY:2A=♂, (*b*) in *B. alba*, which is a homozygous strain, all individuals are females modified to give staminate flowers by a male-determining mutation in an autosome, (*c*) XX:A^mA^m=hermaphrodite. All the progeny of the cross *B. dioica* ♀ × *B. alba* ♂ would be XX:AA^m and are females with a tendency to produce male flowers. In the reciprocal cross the females would be XX:AA^m but the males would be XY:AA^m and therefore 'stronger' than *B. dioica* males.

In maize, which is normally monoecious, a dozen and more mutations have been found which modify the expression of sex (Emerson, 1924, 1932). By the use of certain of these dioecious strains of maize have been produced. These mutants provide strong support for the conception that the sex-characters are the product of the action of many genes, some male-determining and some female-determining, the end result being decided by the interplay between these two kinds.

In *Rumex acetosa* Ono (1935) has described the occurrence of triploidy. The normal diploid female has 14 chromosomes, XX:6 pairs of autosomes. In the male there are the same 6 pairs plus XYY. Individuals with the constitution 2X+2Y+3A were found to be intersexes. In this species the sex-determining genes on the X are predominantly female-determining, those on the autosomes predominantly male-determining, and the Y is neutral.

CHAPTER 7

SPECULATIONS CONCERNING THE EVOLUTION OF THE SEX-DETERMINING MECHANISM

It is possible that at a certain stage in the history of the earth the conditions essential for the appearance of life presented themselves, never afterwards to be repeated, peculiar in respect of temperature, pressure, of the composition of the waters and of the gases in the atmosphere above the waters. It is possible that the conditions at that time existing led to the appearance of living matter as inevitably as earlier and different sets of conditions had led to the formation of the seas and the rocks.

The first living or half-living things which appeared in the waters were possibly large molecules synthetized under the influence of the sun's radiation and capable of reproduction only in this particularly favourable medium.

A review of living things now known to us permits us to assume that the enzyme, the virus and the bacteriophage are perhaps milestones along the beginning of the road that life has passed onwards and upwards toward its inevitable destiny. If they cannot be seen they can be recognized and counted by the effects they produce. Muller (1929) has suggested that the bacteriophage is a gene.[1] It may well be that life remained in this stage of its development for many millions of years before a suitable assemblage of similar units was brought together in the first cell. There must have been innumerable failures, but the first successful cell which consisted of numerous half-living chemical molecules suspended in water and enclosed in an oily film found plenty of food and an immense advantage over its competitors. From this original simple colloidal complex to the first and simplest unicellular organism known to the biologist is a

[1] For a fuller account of bacteriophage and of its nature the reader is referred to Dr. Gardner's excellent monograph on Microbes and Ultramicrobes in this series.

step as vast as that which separates the latter and man. We know nothing of this grand procession; we can but conjecture that it was punctuated by the development of various precise mechanisms. From what we know of the gene today we can surmise that the earliest genes consisted of molecules capable of determining the formation of similar particles and also of dissimilar particles. We may assume that reproduction by simple division attended upon growth and that every few hours a new generation of these units was subjected to the appraisal of the selecting factors in the changing environment. At some stage in this eventful history there must have come a time when the gene, dividing, became two which did not separate but which remained together so that the beginnings of a gene company would be evolved. Since we know that genes in such a company can mutate independently, it follows that through the increasing complexity thus resulting advantages possessing a survival value would be conferred upon the individual.

The benefits of gene association must then have been made more permanent by the development of mitosis, which development would take the form of the establishment of a mechanism which ensured the synchronous division of all the genes. Thus the nucleus would be evolved and within it the gene associations would become linear and the chromosomes would be formed, and, for their exact division, the centrosome, spindle and the spindle attachment would be evolved. Fragmentation, with the development of new spindle attachments, translocation, together with frequent gene mutation, would slowly, surely, build up permanent gene associations which would yield different types of genic balances to be appraised and selected. At this stage, sexual reproduction would appear, possibly as a result of a gene mutation which made the fusion of two individuals inevitable. Following upon this, meiosis—a modification of mitosis—must have appeared, bringing with it two exceedingly great advantages; the maintenance of constancy in chromosome number and the provision of the conditions of crossing over with consequent recombination of genes and reconstruction within the chromosome. It may

be assumed that originally this modification of mitosis applied to all mitoses in the organism. Later developments would be restriction of meiosis in time and in space. Ultimately, as living types evolved, it would be restricted to certain events in gametogenesis, and the gametes would come to be constitutionally haploid cells, and the diploid-haploid mechanism would be perfected.

Next, it may be assumed, came a differentiation of the gametes to yield one kind that was fertilized and another that fertilized. Then followed the development of homo-hetero-gamety, one type of individual becoming so equipped that perforce it must elaborate two kinds of gametes. This probably was affected by development which reduced crossing over. It is established that, in Drosophila at least, there are genes which can and do reduce or even suppress crossing-over. The suppression of crossing-over means that qualitative differences can arise in the members of a chromosome pair, and that these cannot be transferred from one member of the chromosome pair to the other, so that in respect of these qualitative differences the individual maintains a constitutionally heterozygous condition. It is established, further, that reduction of crossing-over in the case of one pair of chromosomes is attended by a similar reduction of crossing-over in the case of all the rest of the chromosomes within the chromosome complex. It may be assumed that this suppression of crossing-over occurred in the case of a pair of chromosomes which later were to become the sex-chromosomes. As a result of this suppression, two chromosomes would evolve independently of one another and would ultimately come to lose all qualitative relationship. Following upon this would come quantitative differences between the members of the sex-chromosome pair. At first the members of this pair would be alike in external structure. Part of one of them which, because of a non-homology, could no longer pair with the corresponding portion of the other, would become deleted so that there would now remain an X-chromosome and a Y. The Y-chromosome, by further deletion, would become smaller and smaller, and finally the whole of it would be eliminated.

The qualitative-quantitative differentiation of the sex-chromosomes has actually been observed in every stage of development from their behaviour at prophase, their relative size at metaphase, and their behaviour at meiosis.

The differentiation of the sex-chromosomes would be followed by important genetic effects. Since mutations within a chromosome can only be tested in different combinations when they can be freely distributed by crossing-over, suppression of crossing-over prevents mutations occurring in the Y from being so tested. Since crossing-over does not occur, the Y cannot undergo any structural change by means of interchange of parts. The Y-chromosome, therefore, during its evolution, would come to lose its effectiveness in the matter of sex-determination, and its place would be taken by the autosomes interacting with the X.

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GLOSSARY

ALLELOMORPH. *Allelon*, one another; *morpha*, form. One of a pair of alternative hereditary characters. The term is also applied to those genes which can occupy one and the same locus upon a particular chromosome.

ANAPHASE. *Ana*, up; *phasis*, appearance. The stage at which daughter chromosomes move apart in nuclear division.

ATTACHMENT. (1) The spindle attachment, q.v. (2) The permanent fusion of two chromosomes (catination).

AUTOSOMES. *Autos*, self; *soma*, body. Those chromosomes in respect of which both sexes are alike.

BALANCE, GENIC. The condition in which the genes are so related and proportionally adjusted that in their action they yield normal development of the organ.

BIVALENT (see Univalent). *Bis*, twice; *valere*, to be worth. A term applied to double chromosomes formed by the coupling of two chromosomes especially in the process of synapsis.

CENTROSOME. *Kentron*, centre; *soma*, body. The self-propagating body which, during mitosis in many organisms, lies at the two poles of the spindle and appears to determine its orientation.

CHROMOSOMES. *Chroma*, colour; *soma*, body. Separate, deeply-staining bodies commonly rod-shaped or loop-shaped into which the substance of the nuclear network resolves itself during mitosis and from which the nucleus is derived at the end of mitosis.

CROSSING-OVER. The exchange of corresponding segments between corresponding chromatids of different chromosomes.

DIPLOID. *Diploos*, double. The zygotic number of chromosomes (2n) as opposed to the gametic or haploid number (n).

DISJUNCTION. The separation of chromosomes at anaphase, particularly of the first meiotic division.

FIRST DIVISION. The first of two meiotic divisions; the heterotypic or reduction division.

GAMETE. *Gametes*, spouse. Cells which are specialized for fertilization and which normally cannot develop without it.

GENE. *Gen*, to produce or producing. The unit of Mendelian heredity; a hypothetical elementary entity which determines the development of a particular character. To the student of heredity it is that which the atom is to the chemist.

GENOTYPE. *Genus*, a race; *typus*, an image. (1) The genetic constitution of an individual. (2) A class or group all the individuals within which are identical in their genetic constitution.

GYNANDROMORPH. *Gyne*, woman; *aner*, man; *morphe*, form. An individual exhibiting a combination of male and female characters.

HAPLOID. *Haploos*, single. Applied to the reduced or gametic number of chromosomes.

HAPLO-DIPLOID SYSTEM. That in which the sexes are distinguished in that one is haploid, the other diploid.

HERMAPHRODITE. *Hermaphroditos*, combining both sexes. An organism with both male and female reproductive organs.

HETEROGAMETIC. *Heteros*, other; *gametes*, spouse. Elaborating gametes of two kinds in respect of the elements of the sex-determining mechanism.

HETEROKINESIS. *Heteros*, other; *kinesis*, change or movement. That meiotic division in the course of which the sex-producing gametes become separated by differential distribution of the sex-chromosomes.

HETEROPYCNOSIS. *Heteros*, other; *pyknos*, dense. Precocious condensation of certain chromosomes in the prophase especially of meiosis.

HETEROTYPIC DIVISION. The first meiotic division (falling into disuse).

HETEROZYGOTE. *Heteros*, other ; *zygon*, yolk. A Mendelian hybrid in whose genetic constitution there are one or more recessive genes and which, therefore, does not breed true. The offspring of a mating of parents which differed one from the other in respect of one or more allelomorphic characters.

HOMEOTYPIC DIVISION. The second division of meiosis (falling into disuse).

HOMOGAMETIC. *Homos*, alike; *gametes*, spouse. Elaborating gametes all of a kind in respect of the elements of the sex-determining mechanism.

HOMOZYGOTE. *Homos*, alike; *zygon*, a yolk. An individual in whose genetic constitution each gene is present in the duplex state. The offspring of a mating of two parents genetically identical in respect of one or more Mendelian characters.

KARYOGAMY. *Karyon*, nucleus; *gametes*, spouse. Fusion or nuclei at the fertilization of an egg by a sperm.

KARYOKINESIS. *Karyon*, nucleus; *kinesis*, change or movement (=mitosis).

MATRICLINOUS. *Mater*, a mother. Inclining heredity toward the maternal side.

MATURATION. The ripening or final stages in the formation of the gametes by meiosis.

MEIOSIS. *Meiosis*, reduction. A form of mitosis in which the nucleus divides twice and the chromosomes once.

MIDDLE PIECE. A term of vague meaning applied to the middle region of the sperm.

MITOSIS. *Mitos*, a thread. The process by which the daughter chromosomes are separated into two groups.

NON-DISJUNCTION. The failure of separation of paired chromosomes at meiosis and their passage to the same pole.

OOCYTE. *Oön*, an egg. The egg cell prior to the completion of the maturation process.

OOGENESIS. Gametogenesis in the female.

PARTHENOGENESIS. *Parthenos*, a virgin. The development of an egg without activation of a sperm.

PATRICULINOUS. *Pater*, a father. Inclining heredity toward the paternal side.

PHENOTYPE. *Phainein*, to appear; *typos*, an image. (1) The sum of the characters exhibited by an individual. (2) A group or class composed of individuals all of whose characters are alike.

POLAR BODY. The expelled products of the two divisions of the oocyte nucleus in animals.

POLYPLOID. *Polys*, many; *aploos*, one-fold; *eidos*, form. An organism with more than two sets of homologous chromosomes.

REDUCTION. The halving of the chromosome number at meiosis.

SEGREGATION. The separation of chromosomes of paternal and maternal origin at meiosis. Genetically, the separation during the course of a breeding experiment of the alternative allelomorphic characters involved.

SEX-CHROMOSOMES. Chromosomes in respect of which the sexes differ.

SPERMATOCYTE. *Sperma*, a seed; *hytos*, a cell.

SPERM, SPERMATOZOON. The male gamete in animals.

SPERMATOGENESIS. Gametogenesis in the male.

SYNAPSIS. *Synapto*, to fuse together. Chromosome pairing at zygotene.

TETRAD. *Tetras*, four. (1) A quartet of cells formed by meiosis in a mother-cell. (2) The four chromatids making up a bivalent at meiosis.

TRIPLOID. An organism having three sets of chromosomes.

UNIVALENT. A body at the first meiotic division corresponding with a single chromosome.

X-CHROMOSOME. A sex-chromosome of which one sex possesses one, the other two.

Y-CHROMOSOME. The sex-chromosome which is the mate of the single X in the heterogametic sex.

ZYGOTE. *Zygotes*, yolked. (1) The cell formed by the union of the gametes in the fertilized egg. (2) The individual derived therefrom.

ZYGOTENE. *Zygon*, yolk; *taenia*, a thread. The pairing threads and the stage at which they occur in the prophase of meiosis.

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